

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference NBI07.0240PC	FOR FURTHER ACTION	See item 4 below
International application No. PCT/US2007/086380	International filing date (<i>day/month/year</i>) 04 December 2007 (04.12.2007)	Priority date (<i>day/month/year</i>) 04 December 2006 (04.12.2006)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant NEUROCRINE BIOSCIENCES, INC.		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 <i>bis</i> .1(a).																								
2.	This REPORT consists of a total of 8 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 30%;">Box No. I</td> <td style="width: 60%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date of issuance of this report 10 June 2009 (10.06.2009)
Facsimile No. +41 22 338 82 70	Authorized officer <div style="text-align: center; font-weight: bold; margin-top: 10px;">Nora Lindner</div> e-mail: pt11.pct@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2007/086380

International filing date (day/month/year)
04.12.2007

Priority date (day/month/year)
04.12.2006

International Patent Classification (IPC) or both national classification and IPC
INV. C07D401/14 C07D403/04 C07D403/14 C07D405/14 C07D409/14 C07D413/04 C07D413/14 C07D417/14
C07D487/04 C07D491/10 A61K31/506 A61P25/00

Applicant
NEUROCRINE BIOSCIENCES, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2007/086380

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2007/086380

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 1-22(part)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 1-22(part) are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

see separate sheet

☐ no international search report has been established for the whole application or for said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13^{ter}.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2007/086380

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	<u>1-22</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-22</u>
Industrial applicability (IA)	Yes: Claims	<u>1-22</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Present claims 1-22 relate to an extremely large number of possible products and their use.

Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for only a small proportion of the structural variants claimed. The non-compliance with the substantive provisions is to such an extent, that the search of the subject-matter claimed had to be restricted to those products which appear to be supported and a generalisation of their structural formulae (PCT Guidelines 9.19 and 9.23), i.e.

compounds (I) as defined in claim 1, with the restriction that R^2 designates a heterocycle substituted by 0 to 4 R^4 groups, and, at the same time the term "heterocycle" employed in the definition of R^1 is restricted to the meaning thereof as given in claim 2.

pharmaceutical compositions thereof and methods of treatment involving these compounds.

Claims or parts thereof relating to inventions in respect of which no International search Report has been established need not be subject of the Written Opinion of the International Searching Authority (Rule 43bis.1(b) PCT in combination with Rule 66.1(e) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- D1: WO 2006/110884 A (NEUROCRINE BIOSCIENCES INC [US]; ALMIRALL PRODESFARMA SA [ES]; SLEE DE) 19 October 2006 (2006-10-19)
- D2: WO 2005/058883 A (ALMIRALL PRODESFARMA SA [ES]; CRESPO MARIA ISABEL [ES]; PRAT QU) 30 June 2005 (2005-06-30)
- D3: EP-A-0 407 899 (HOECHST AG [DE] HOECHST SCHERING AGREVO GMBH [DE])

16 January 1991 (1991-01-16)

D4: KABBE: "Substituierte 4-Hydroxy- und 4-Amino-pyrimidine" JUSTUS LIEBIGS
ANNALEN DER CHEMIE, vol. 704, 1967, pages 144-149, XP008090403

The patentability of claims 19-22 is inter alia dependent upon their formulation as well as upon national and regional laws, and no unifying criteria is provided in this field in the PCT. Their assessment will be carried out based on the alleged effects of the compounds/compositions searched in the international Search Report.

The compounds 9.8, 9.9, and 9.16 disclosed in D3 (p. 33-34) as well as the compound 5 disclosed in D4 are representatives of the compounds claimed in the present case.

The disclosure of these documents takes away the novelty of claims 1-2 and 14 (Art. 33(2) PCT).

D3 and D4 are accidental disclosures, as none of these documents suggests an eventual medical use of the compounds described therein.

The subject-matter claimed in the present case significantly overlaps with the subject-matter claimed in D1 and D2. Most of the compounds exemplified in these two documents are representatives of the compounds (I) claimed in the present case.

D1 and D2 furthermore teach the same potential pharmacological use of the compounds disclosed therein as that of the compounds (I) of the present application, i.e. their alleged function as adenosine receptor antagonists and thus their suitability for the treatment of certain conditions such as Huntington's and/or Parkinson's disease.

The subject-matter of claims 1-22 is, by consequence, neither novel (Art. 33(2) PCT) nor inventive (Art. 33(3) PCT).

Further objections:

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D4 is not mentioned in the description, nor are these documents identified therein.

The relative term "lower" used in the claims is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of the claims concerned (as well as that of the claims dependent therefrom) unclear (Article 6 PCT).

The term "pharmaceutically acceptable ester" used in claim 1 is a functional definition and does not provide the skilled person with the necessary teaching for assessing what subject-matter is actually comprised therein.

By using the term "pharmaceutically acceptable ester" it is also attempted to define the invention by a result to be achieved which is not allowable (cf. also PCT International Preliminary Examination Guidelines III-4.7).

The subject-matter of claim 1 therefore does not fulfil the requirements of Article 6 PCT.

The vague and imprecise expression "spirit" employed in the description on page 52 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).